and was told that he had suddenly died, a course of events common enough in this disease. However, in the dead man's home I met a friend and colleague of his, whose story of the patient's last moments was as follows. Both policemen were out on duty when my patient had a sudden attack of severe pain in the chest. He was on the point of collapsing, but, supported by his friend, he just managed to remain standing, pale and bathed in sweat. Nitroglycerin did not alleviate the pain. When his friend proposed taking a taxi to the hospital, he refused, saying: "Since we have started on foot, we shall go on foot. There is no pain in the world strong enough to make me stop." He managed to walk the distance of about 400 m. to his home and even to mount four flights of stairs to his flat on the second floor, the lift being out of order. Then, having opened the front door, he fell down dead.

It is a well-known fact that mortality from acute myocardial infarction is much higher among men than among women. In Finland the average life-span of men is, according to Kannisto (1951), 6.5 years shorter than that of women. Kannisto came to the conclusion that this difference between men and women, which is apparently greater in Finland than anywhere else, is largely due to the high mortality of middle-aged and old Finnish males from cardiac trouble. Among the causes of death acute myocardial infarction is of especial significance. The present investigation shows that there is a remarkable difference in the response of men and women to the symptoms of an attack, and to the pain of angina pectoris, and it may well be that this difference in part accounts for the high mortality from acute myocardial infarction among men in Finland.

Summary

A report is presented on the physical exertions of 102 men and 31 women immediately after the onset of acute myocardial infarction.

Only 28% of the men stopped all physical activity at once or soon after the onset of the attack. The majority (72%) continued to be active in spite of intense pain, even walking considerable distances, remaining at work, and so on. It was obvious that in many cases they had been able to keep up their efforts only by straining their will-power to the utmost. But even the severest pain did not seem to be a strong enough check to prevent them from moving.

The majority of the women (about 77%) went to rest immediately at the onset of the attack under the compulsion of the symptoms.

The response of the men was as unwise among those under 60 as among those over 60 years of age. The men who had had a previous myocardial infarction or previously diagnosed coronary insufficiency were only slightly more prudent. However, the view was taken that something might be gained by instructing patients more carefully.

It is suggested that the physical activity continued by men in spite of the symptoms of the attack may be a contributory factor in the mortality from acute myocardial infarction.

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METASTATIC ARGENTAFFINOMA SECRETING 5-HYDROXYTRYPTAMINE IN A PATIENT WITH A PATENT FORAMEN OVALE

BY

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Evidence has recently accumulated that 5-hydroxytryptamine (5-H.T.) is a specific product of the enterochromaffin cell (Barter and Pearse, 1953; Erspamer, 1954), and many of the signs and symptoms associated with carcinoid tumours seem to be directly attributable to the release of large amounts of this substance into the circulation (Page, 1958). There are, however, some facts which are not readily explicable in terms of 5-H.T. mediation. For example, the valvular and endocardial changes which are almost always associated with carcinoid with flushing attacks cannot with certainty be accounted for by 5-H.T. Some carcinoid patients exhibit a histamine-like flush which is greatly reduced by antihistamine drugs. They may also have histaminuria (Waldenström *et al.*, 1956). In others, diarrhoea, which is usually a severe symptom, is absent. It has been reported that some carcinoids contain little or no 5-H.T., and the suggestion has been made that these may constitute a group secreting 5-hydroxytryptophan (5-H.T.P.) rather than 5-H.T. (Sandler and Snow, 1958). Lastly, Lembeck (1954) has presented evidence of the presence of large amounts of a pharmacologically active substance in a carcinoid tumour in addition to 5-H.T. The studies on the present case are presented with these points in mind.

Case Report

An able seaman, aged 26, while serving in the Roval Navy in Malaya in 1951 became aware of recurrent attacks of flushing which mainly involved his face. Attacks of diarrhoea, associated with colicky pain in the right iliac fossa, began the following year and eventually became so severe that he was invalided home. Because these attacks persisted and became increasingly severe he was admitted to hospital in 1954, as a possible case of amoebic dysentery, but evidence of this infection was never found. At this time the heart was normal, and an *x*-ray examination of the chest showed no evidence of either pulmonary or cardiac disease. Because of further attacks of pain he was admitted to a hospital in Epsom in 1955, as a possible case of chronic appendicitis. Laparotomy showed that the mesentery was cicatrized, contracted, and filled with discrete softish glands, but some were hard and matted. A number of small discrete white nodules were also noted in the liver. The

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appendix, which was normal, was removed. Though the condition was regarded as neoplastic, only non-specific inflammatory changes were noted in a piece of material sent for microscopy. A subsequent barium enema showed deformity of the caecum, and at this point he was given a course of corticotrophin with marked symptomatic relief. After his discharge from hospital he remained disabled, with recurrent attacks of diarrhoea, vomiting, and abdominal pain, and was admitted in February, 1956, to the Hospital for Tropical Diseases under the care of Sir George McRobert.

On examination he was found to have a marked facial flush. The liver was enlarged and irregular, and a hard mass was palpable in the right lower abdominal quadrant. Along the lower left sternal margin a moderately loud systolic murmur could be heard, increasing on inspiration, with a thrill. A short mid-diastolic murmur, audible during inspiration, was also present. At the pulmonary area there was a faint systolic murmur, with normal splitting of the second sound. Phonocardiography confirmed these findings. Screening of the heart showed slight dilatation of the right auricle. The pulmonary artery, which was just visible, was pulsating well and appeared normal. The electrocardiogram showed no abnormality. An excess of 5-hydroxyindolacetic acid (5-H.I.A.A.) was found in the urine, and the blood level of 5-H.T. was grossly increased. A diagnosis of a metastasizing argentaffin tumour and tricuspid incompetence with stenosis was made.

Progress

The diagnosis was confirmed on February 8, when he was transferred to University College Hospital with acute intestinal obstruction. At laparotomy the terminal 4 ft. (122 cm.) of the ileum was gangrenous, the vascular occlusion being due to scarring of the mesentery and a great mass of hard matted glands in the ileocaecal angle. The gangrenous small bowel, together with the right half of the colon, was resected and normal continuity restored by an end-to-end anastomosis. A small readily accessible secondary deposit in the liver was removed for examination. Severe bronchial spasm throughout the operation caused considerable anxiety. Many flushes, affecting most of the patient's cutaneous surface, were observed during convalescence, and persistent severe diarrhoea was troublesome to the time of his discharge one month later. Microscopy of a lymph node from the operation specimen showed secondary argentaffinoma.

He had been out of hospital only a fortnight when he was again admitted with widespread oedema. Injections of mersalyl produced a profuse diuresis; treatment, initially with blood and plasma transfusion, and subsequently with a high-protein low-salt diet, controlled the oedema. After his discharge, though troubled by diarrhoea and fluid swellings of various parts of the body, he was able to do light work during the next five months. He had to be readmitted in September, 1956, because of persistent severe diarrhoea and a nutritional disturbance resembling pellagra. During the three months he was in hospital attempts were made to measure his response to treatment with 5-H.T. antagonists and possible metabolic competitors. Assessment was complicated for two reasons. He improved symptomatically on a balanced diet alone, and there was an episode of acute congestive cardiac failure during the period of observation.

The results of the investigations, which were under the direction of Professor Dent, suggested that tryptophan might be present in insufficient amounts for normal requirements. This conclusion was based on the results of urinary nitrogen determinations, which fell from about 5 g. to 3 g. a day on giving an oral supplement of tryptophan. Furthermore, the patient was found to have an almost complete inability to excrete sodium under normal conditions, although the output was greatly increased by mersalyl. His treatment on discharge consisted essentially of digoxin, mersalyl, and nicotinamide. Recurrence of his oedema, swelling of the genitalia which led to mechanical obstruction of micturition, and persistent severe diarrhoea little influenced by oral hexamethonium bromide and mist. creta cum opio, brought him back into hospital within three weeks of his discharge. Little other than symptomatic treatment could now be given. Circumcision relieved the difficulties of micturition, but severe bronchial spasm during the operation nearly led to his death. Miserable, and worn out with persistent tachycardia and severe intractable diarrhoea, he gradually deteriorated, dying in May, 1957.

Post-mortem Findings

Marked changes were found in the right side of the heart; also gross endocarditis with incompetence of the tricuspid valve and an early pulmonary stenosis with thickening and rolling of the edges of two of the valve cusps. A small patent foramen ovale was present. The edges of the mitral valve showed early thickening, and there was white capping of the papillary muscle. Pulmonary metastases were not observed, nor was the primary tumour found anywhere in the gut. The hepatic metastases had not greatly increased in size or number since operation.

Histology of Tumour Metastases.—On section the metastases were yellowish in colour. When stained with an ammonium-silver impregnation (Masson–Fontana procedure) the cells were strongly argentaffin. There was typical palisading around a central mass of grey round cells.

Biochemical and Pharmacological Observations

5-H.I.A.A. and Histamine in Urine and 5-H.T. in the Blood

The excretion of 5-H.I.A.A. in the urine was determined by the method described by Macfarlane *et al.* (1956) and the concentration of 5-H.T. in the blood by that described by Hardisty and Stacey (1955). Urinary histamine was determined by the method of Roberts and Adam (1950). The values for histamine in the urine and of 5-H.T. in the blood were obtained by Dr. R. S. Stacey and are gratefully acknowledged. The tests were performed several weeks after laparotomy.

The 5-H.T. concentration of whole venous blood was 2.2 and 2.6 μg./ml. respectively on two separate occasions. This is much higher than the normal values of 0.16 ± 0.06 μg./ml. in man (Snow *et al.*, 1955), and is of the order of the highest concentration reported in patients with carcinoid tumours (Stacey, 1957).

5-H.I.A.A. determinations were regularly done on 24-hour urine samples for a period of two weeks. The urine excretion varied from 75 to 150 mg./24 hours, a figure greatly in excess of 7 mg./24 hours found to be the mean excretion in a group of normal controls (Macfarlane *et al.*, 1956). The 24-hour histamine output in the urine was on one occasion 7.0 μg./24 hours. This amount is in the lower range of normal histamine excretion (Roberts and Adam, 1950), and is in contrast to the value of 1,100, 1,800, and 3,600 μg./24 hours reported by Macfarlane *et al.* (1956) in 3 of their 19 cases.

Analysis of Hepatic Metastases

Methods.—A liver metastasis weighing 730 mg. was obtained at operation and frozen. It was freeze-dried without thawing and then ground into a fine powder weighing 160 mg. For pharmacological testing the powder was extracted with Tyrode solution and the *p*H adjusted to 3–4 with hydrochloric acid, neutralized, and tested on the smooth-muscle preparation. For paper chromatography 12–15 mg. of freeze-dried tumour was extracted three times with 1 ml. of 95% ethanol. The extract was dried *in vacuo* and taken up in 0.25 ml. H_2O. The supernatant fluid was reduced to a small volume *in vacuo*, and placed as a narrow 1 cm. strip on Whatman No. 1 paper. A marker of 5-H.T. (10–20 μg.) was simultaneously run. Ascending chromatograms were run overnight at room temperature in *n*-butanol/acetic acid/water (Partridge, 1948) and isopropanol/hydrochloric acid (Lembeck, 1954) solvents. The

paper was examined under an ultra-violet lamp, cut into parallel horizontal strips 1 cm. wide, eluted with Tyrode solution, and tested on the isolated muscle preparation. Guinea-pig ileum or rat uterus strip was suspended in Tyrode solution at 35° C. and 26–28° C. respectively. Atropine, mepyramine, and lysergic acid diethylamide (L.S.D.) were used as antagonists in a concentration of 10^{-4} g./l. when required. Details of these methods are described by Holdstock *et al.* (1957).

Results.—Extracts of freeze-dried tumour metastases tested on the isolated guinea-pig ileum and rat uterus contained approximately 850 μg. of 5-H.T./g. of tumour. There was no significant action of smooth muscle which was not due to 5-H.T. The activity of the extract was completely abolished by L.S.D. Tests for histamine failed to reveal its presence in the tumour, the amount being less than 10 μg./g. of freeze-dried tumour. This is much less than the reported histamine content of the intestinal mucosa in man (Feldberg, 1956) and would indicate that the argentaffin cell is not a source of mucosal histamine. Eluates of paper chromatograms of tumour extract possessed pharmacological activity in an unbroken band on the paper corresponding in R_f with the 5-H.T. marker strip and indistinguishable from 5-H.T. in pharmacological properties. The same result was obtained in *n*-butanol/acetic acid and isopropanol/hydrochloric acid solvents and when the eluates were tested on either the guinea-pig ileum or rat uterus. In no instance was any pharmacological activity detected other than that satisfactorily accounted for by 5-H.T. In our experience, acid extracts of the tumour as described by Lembeck (1954) were not suitable for chromatography. With such extracts the 5-H.T. remained partly at the point of application and the remainder was found "smeared" over the paper, probably because of the high concentration of impurities.

Discussion

Our observations on this patient are in accord with the hypothesis that the severe diarrhoea and antihistamine-resistant vascular phenomena were mediated by the release of 5-H.T. into the circulation from the secondary argentaffinomata in the liver. The absence of histamine or other active substances from the tumour tissues makes it unlikely that histamine is present in the argentaffin cell or that it contributed to the diarrhoea or flushing seen in this patient. The finding of Lembeck (1954) that the liver metastases from a carcinoid tumour contained a pharmacologically active substance in addition to 5-H.T. was not found in these metastases, although various chromatographic and assay procedures were employed. Our findings in this respect are similar to those of Giarman *et al.* (1957), who examined similar metastases. It is possible that the second substance in Lembeck's experiments was an artifact of the chromatographic procedure, particularly since it was not distinguished from 5-H.T. by properties other than R_f value in the chromatography of a crude extract.

From a study of their own patient and a review of reported cases, Sandler and Snow (1958) suggested that carcinoid tumours consist of at least two histologically and "chemically" distinct types of cells—namely, argyrophil and argentaffin—secreting 5-H.T.P. and 5-H.T. respectively. The high urinary 5-H.T. excretion in the former instance would be due to the conversion of the secreted 5-H.T.P. by tryptophan decarboxylase in the kidney and the other tissues (Clark *et al.*, 1954; Gaddum and Giarman, 1956). Histaminuria and a histamine-like flush appear also to be associated with the 5-H.T.P.-secreting tumours, and Sandler and Snow suggest that significant amounts of histamine may be released from various tissues by circulating 5-H.T., which has a histamine-releasing effect on cat skin (Feldberg and Smith, 1953). In our patient, however, the flushing reaction was a mottled cyanosis, unlike that caused by histamine, and it was unaffected by antihistamine drugs. Furthermore, the tumour tissue did not contain detectable amounts of histamine.

Though our investigations cannot be extended to other possible types of carcinoid, it should be remembered that the release of histamine from skin is accompanied by pruritus and urticaria or angio-oedema in addition to erythema, in animals and in man (Paton and Schachter, 1951; Lecomte, 1956). Pruritus or urticaria has not been reported as an accompaniment of flushing in patients with carcinoid. In man, the intradermal injection of 5-H.T. fails to increase capillary permeability to circulating dye (Herxheimer and Schachter, 1959), which makes it unlikely that 5-H.T. releases histamine from human skin. The possibility that some tumours involve a cell type which secretes histamine must be considered. As yet, however, the few carcinoids examined with this in mind have not been reported to have a high histamine content.

There is as yet no satisfactory explanation for the pathogenesis of the valve lesions. The right side of the heart is the most affected, the left being relatively immune in most reported cases. Though the exact mechanism giving rise to the cardiac damage is unknown, a possible reason for this localization is suggested by Goble *et al.* (1956), who have shown in a patient with the fully developed syndrome that two-thirds of the free 5-H.T. in the blood is removed in its passage through the lungs. In the present case there was no history indicative of cardiac disease until general symptoms associated with carcinoid appeared. The patient, classified as fit for general service, had served in the Royal Navy. During an admission to hospital in 1954 his heart was found to be normal, and an *x*-ray examination of the chest showed no evidence of cardiac disease. By 1956 he had developed signs of tricuspid incompetence and stenosis. His first attack of congestive cardiac failure occurred later in the same year, eight months before he died in May, 1957. During this latter period the possibility of surgical alleviation of the severely crippled heart was considered, but because the exact cardiac lesion was unknown the idea was abandoned.

At necropsy marked changes were found in the right side of the heart. There was gross endocarditis with incompetence of the tricuspid valve and an early pulmonary stenosis with thickening and rolling of the edges of two of the valve cusps. An unusual finding was a small patent foramen ovale, which, in the absence of pulmonary metastases, probably accounted for the early thickening of the edges of the mitral valve. An identical anatomical case has recently been studied by McKusick (1956). The occurrence of mitral stenosis as well as pulmonary stenosis in the presence of a patent foramen ovale strongly supports the view that there is a humoral factor producing the lesion. It has been claimed that carcinoid tumours develop from embryonic rests, and it might be that the pulmonary stenosis is a congenital abnormality.

The gross endocarditis seen in this patient and described in others by McKusick (1956) and Thorson *et al.* (1954) does not occur in congenital stenosis. Post-mortem study of the valves indicated no similarity to specific diseases such as syphilis or rheumatic fever,

and the changes were quite different from those of congenital stenosis. It would seem, therefore, that the pathogenesis of the cardiac and valvular lesions was secondary to the release of 5-H.T. or to some other chemical substance directly or indirectly associated with the tumour tissue. Because cardiac failure appears to occur late in the disease, by which time the heart is damaged by multiple lesions—the most frequent of these being endocarditis, pulmonary stenosis, and tricuspid incompetence—cardiac surgery is likely to have only a very limited field of application in the treatment of these cases. On the other hand, extirpation of tumour tissue in an attempt to shield the heart from the baneful effects of 5-H.T. might in some circumstances be worthy of consideration.

Oedema was a most incapacitating and troublesome symptom. Not always in dependent parts, sometimes confined to the face and thighs, it occasionally became widespread. It appeared shortly after resection of the gangrenous terminal ileum. During the patient's convalescence from this operation a persistently low urinary output, in spite of adequate fluid intake and a sudden inexplicable gain of 6 lb. (2.7 kg.) in weight, preceded the onset of widespread oedema, which brought him back into hospital only 10 days after discharge. On this and subsequent occasions repeated observations of the blood pressure did not reveal any significant deviation from the normal. Mersalyl produced a profuse diuresis followed by a rapid disappearance of the oedema of the soft parts, the small bilateral pleural effusions, and the ascites. For the remaining year of his life a varying degree of oedema was associated with severe thirst and oliguria, the 24-hour urinary output persistently bordering upon 500 ml. or considerably less. It was only by weekly injections of mersalyl, the response to which was always dramatic, that he could be prevented from becoming waterlogged.

Though the antidiuretic effect of 5-H.T. has been questioned by Abrahams and Pickford (1956), it is regarded by Erspamer (1954) as a normal and important function of this substance in the body. Smith *et al.* (1957) found that the kidney was in fact able to deal with the water load in four of their cases, the study of which led them to suggest that the antidiuretic effect of 5-H.T. was inconstant because its effect upon the kidney was indirect and mediated by vascular change. Various stages of infarction of the kidneys presumably due to renal vasoconstriction have been reported in rats to which 5-H.T. was administered subcutaneously (Hedinger and Langemann, 1955; Page and Glendening, 1955). Our patient was unable to excrete sodium under any normal conditions, the 24-hour output averaging about 1 mEq. On two occasions when mersalyl was given the output immediately increased to 300 and 600 mEq, falling again to the control level within two days. Sodium retention appeared to be the immediate cause for the oliguria and persistent oedema. This would be in accordance with the observations of Hulet and Perera (1956), who have shown that the administration of 5-H.T. may be associated with significant sodium retention.

Diarrhoea, which appears to be due to increased motility consequent upon the local effect of 5-H.T. on the gastro-intestinal tract, has been little emphasized in the descriptions of the syndrome. It was this patient's principal complaint, and caused him great misery. Though it started in attacks during 1952, it was not until 1956 that it became persistent, severe, and resistant to all forms of treatment. Shortly after the onset of the severe symptoms a pellagra-like state became manifest. He became very depressed, irritable, and morose, was easily upset, and resented any interference or examination. He had a red sore tongue, and complained bitterly of severe burning pain in the rectum, great weakness, loss of muscle bulk, and cramps and pains in the legs. During this time, on giving tryptophan, there was a steady and almost certainly significant fall in the total urinary nitrogen output from about 5 to 3 g. a day, suggesting that tryptophan might have been present previously in insufficient quantities for total utilization of dietary protein.

Tryptophan, an essential amino-acid, is required not only for protein synthesis but also as a precursor of nicotinic acid. 5-H.T. is also derived from tryptophan, but in normal circumstances it is a minor metabolic pathway of tryptophan metabolism (Udenfriend, 1958). In the presence of an argentaffinoma the production of 5-H.T. is enormously increased and the major portion of the dietary tryptophan may be utilized in this way. This metabolic parasitism of the tumour was thought to be primarily responsible for the observed nutritional disturbance, which was further exacerbated by the severe diarrhoea. It is interesting to compare this situation with that occurring in Hartnup disease (Baron *et al.*, 1956), where a pellagra-like state may intervene owing to an inborn error of metabolism which causes wastage of dietary tryptophan along a rather different pathway.

Summary

A case of metastatic argentaffinoma with high urinary excretion of 5-hydroxyindolacetic acid and elevated blood 5-hydroxytryptamine excretion is described. There was no evidence of altered histamine metabolism.

The tumour metastases were found to contain high concentrations of 5-hydroxytryptamine, but no other smooth-muscle stimulant was detected.

The damage to the mitral valve as well as tricuspid and pulmonary stenosis may be explained on the basis of the patent foramen ovale found at necropsy.

Sodium retention was an unusual feature and appeared to be the immediate cause of oliguria and persistent severe oedema.

A nutritional disturbance resembling pellagra may have been due in part to diarrhoea and in part to nicotinic acid deficiency secondary to abnormal tryptophan metabolism.

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TRANSAMINASE AND LIVER-FUNCTION STUDIES IN INFECTIOUS MONONUCLEOSIS

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Clinical manifestations of hepatitis are infrequent in infectious mononucleosis, though subclinical hepatitis is believed to be common because liver-function tests are usually abnormal. However, the tests most often used to demonstrate impaired liver function, the thymol turbidity and the cephalin-cholesterol flocculation, are those which reflect alterations in serum proteins, alterations for which antibody production might be in part responsible; caution has therefore been exercised in regarding abnormal flocculation tests as evidence of liver damage. Nevertheless, Leibowitz (1953) in a review of clinical, chemical, biopsy, and post-mortem studies concluded that hepatitis was an integral feature of most, if not at all, cases of infectious mononucleosis, a conclusion confirmed by the almost invariable finding of inflammatory changes in the liver in the biopsy studies of Nelson and Darragh (1956) and Sullivan *et al.* (1957).

Wróblewski and LaDue (1956) have shown that the levels of the serum glutamic-oxaloacetic and serum glutamic-pyruvic transaminases (S.G.O.T. and S.G.P.T.) are increased in liver-cell injury, the enzymes being liberated from the damaged liver cells into the blood-stream. They also showed that determinations of these enzymes (though not actually measuring liver-cell function) more sensitively reflect liver-cell damage than do conventional liver-function tests.

Rennie and Wróblewski (1957) studied serum transaminase levels in hepatitis associated with infectious mononucleosis and concluded that most patients with infectious mononucleosis have laboratory evidence of complicating hepatitis, but in a later article Wróblewski (1958) states that infectious mononucleosis usually is accompanied by normal S.G.O.T. and S.G.P.T. activity.

A study of liver function in infectious mononucleosis using serum transaminases and conventional liver-function tests has been in progress since the beginning of 1958, and our observations and conclusions are presented below.

Materials and Methods

Twenty-three consecutive patients presenting with infectious mononucleosis during a period of 12 months were studied. These comprised 15 nurses, 1 medical student, and 3 female and 4 male patients referred by local practitioners. All but three of the patients were hospitalized, two were confined to bed at home, and one patient (Case 18) remained ambulant throughout the course of her illness.

The minimum diagnostic requirements for inclusion in the study were the presence of fever, sore throat, and lymphadenopathy, accompanied at some stage by a blood picture in which at least 50% of the total white cells were lymphocytes, and at least 10% of the total white cells were atypical lymphocytes of the type described by Downey and McKinlay (1923).

The serum heterophil antibody titre (H.A.T.) was determined in all patients and differential absorption performed, using ox red-blood-cell and guinea-pig-kidney suspension (Davidsohn, 1937). An H.A.T. of 1:28 or more, provided that absorption occurred with ox red cells but not guinea-pig kidney, was taken as a diagnostic titre (sero-positive) in this laboratory.

Sera were obtained from all patients as soon as possible after the start of illness and at intervals of three to seven days during its course: 10 patients were followed up at least three months after its onset. The start of illness was defined as the day of onset of sore throat, fever, lymph-node swelling, or gastro-intestinal symptoms.

The following chemical estimations were made: S.G.O.T. (Karmen *et al.*, 1955), S.G.P.T. (Wróblewski and LaDue, 1956), thymol turbidity and flocculation (Maclagan, 1944), colloidal gold flocculation (Maclagan, 1946), zinc sulphate turbidity (Kunkel, 1947), mercuric chloride turbidity (Maclagan *et al.*, 1957), alkaline phosphatase (King and Armstrong, 1934), total bilirubin (Malloy and Evelyn, 1937), and total protein (Van Slyke *et al.*, 1950). The normal values of these tests in the laboratory are given in Table II.

Paper electrophoresis by the hanging-strip method was also performed. 10 μl. of serum was applied to Whatman No. 3 MM filter paper saturated with barbitone buffer (*p*H 8.6, μ 0.05), subjected to a potential difference of 110 v. for 15 hours, and the strips were dried, stained with light green, and scanned, using an EEL scanner.

Clinical Findings

All patients had an illness with fever, sore throat, and lymph-node enlargement always affecting the posterior cervical and sometimes the axillary and inguinal nodes. The illness was in all cases of short duration; the average stay in hospital was 19 days, and all patients